

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

ADE & COMPANY
1700 - 360 Main Street
Winnipeg, Manitoba R3B 1Y1
CANADA

RECEIVED

SEP 28 2004

ADE & COMPANY

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference 85084-503		Date of mailing (day/month/year) 24/09/2004
International application No. PCT/CA2004/000591		International filing date (day/month/year) 19/04/2004
Applicant HER MAJESTY THE QUEEN IN RIGHT OF CANADA AS ...		

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31) 70 340 2040, Telex 551 000 01

Authorized officer

Michela Digiusto

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 85084-503	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, Item 5 below.	
International application No. PCT/CA2004/000591	International filing date (day/month/year) 19/04/2004	(Earliest) Priority Date (day/month/year) 17/04/2003
Applicant HER MAJESTY THE QUEEN IN RIGHT OF CANADA AS ...		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

METHOD AND KIT FOR MELECLAR IDENTIFICATION OF SMALLPOX

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2004/000591

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

Internat.	Application No
PCT/CA2004/000591	

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12Q1/70

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, Sequence Search, WPI Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LOPAREV V N ET AL: "Detection and differentiation of old world orthopoxviruses: restriction fragment length polymorphism of the crmB gene region." JOURNAL OF CLINICAL MICROBIOLOGY. JAN 2001, vol. 39, no. 1, January 2001 (2001-01), pages 94-100, XP002296010 ISSN: 0095-1137 cited in the application the whole document	1-4

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

13 September 2004

24/09/2004

Name and mailing address of the ISA
 European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

Authorized officer

INTERNATIONAL SEARCH REPORT

Internat. Application No
PCT/CA2004/000591

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ROPP S L ET AL: "PCR strategy for identification and differentiation of small pox and other orthopoxviruses" JOURNAL OF CLINICAL MICROBIOLOGY, WASHINGTON, DC, US, vol. 33, no. 8, August 1995 (1995-08), pages 2069-2076, XP002261862 ISSN: 0095-1137 cited in the application abstract</p>	1-8
A	<p>MEYER H ET AL: "Gene for A-type inclusion body protein is useful for a polymerase chain reaction assay to differentiate orthopoxviruses" JOURNAL OF VIROLOGICAL METHODS, AMSTERDAM, NL, vol. 64, no. 2, March 1997 (1997-03), pages 217-221, XP002261865 ISSN: 0166-0934 cited in the application abstract</p>	1-8
A	<p>EP 0 753 581 A (IMMUNO AG) 15 January 1997 (1997-01-15) page 11, lines 15-17; sequence 22</p>	5-8
P, A	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 2003, NIE Z ET AL: "Detection and differentiation of variola virus from other orthopoxviruses using RFLP of the complement regulatory protein gene." XP002296011 Database accession no. PREV200400004661 abstract & ABSTRACTS OF THE INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 43, 2003, page 486, 43RD ANNUAL INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY; CHICAGO, IL, USA; SEPTEMBER 14-17, 2003</p>	1,2

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internati

Application No

PCT/CA2004/000591

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0753581 A	15-01-1997	EP 0753581 A1	15-01-1997

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/CA2004/000591

International filing date (day/month/year)
19.04.2004

Priority date (day/month/year)
17.04.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/70

Applicant
HER MAJESTY THE QUEEN IN RIGHT OF CANADA AS ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tlx 523656 eomu d

Authorized Officer

Bradbrook, D



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/CA2004/000591

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☒ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☒ in written format
☒ in computer readable form
 - c. time of filing/furnishing:
☒ contained in the international application as filed.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/CA2004/000591

Box No. II Priority

1. ☒ The following document has not been furnished:
 - ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ not paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
 - ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
 - ☒ all parts.
 - ☐ the parts relating to claims Nos.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/CA2004/000591

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	3-8
	No: Claims	1-2
Inventive step (IS)	Yes: Claims	5-8
	No: Claims	1-4
Industrial applicability (IA)	Yes: Claims	1-8
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section IV

- 1 The application lacks unity within the meaning of Rule 13.1 PCT, and relates to the following separate inventions:

Invention I: A method for detecting and identifying an orthopoxvirus within a sample by PCR-RFLP analysis of the HA gene; a pair of primers for said method; a kit comprising said primers (claim 3 fully, claims 1,2,5-8 partially).

Invention II: A method for detecting and identifying an orthopoxvirus within a sample by PCR-RFLP analysis of the crmB gene; a pair of primers for said method; a kit comprising said primers (claim 4 fully, claims 1,2,5-8 partially).

- 2 The above inventions are linked only in that they both relate to methods for detecting and identifying an orthopoxvirus within a sample by PCR-RFLP analysis of a specific gene of the orthopoxvirus genome. However, such methods are known in the art (cf D1, D2). Therefore, the aforementioned link cannot be considered a single inventive concept in the sense of Rule 13.2 PCT.
- 3 In the light of the prior art, the problem to be solved by the present application is the provision of alternative methods for detecting and identifying an orthopoxvirus within a sample by PCR-RFLP. This problem is solved separately by each of the 2 inventions, which target different genes for the analysis.
- 4 Due to the fact that no other feature could be identified which might be considered to represent a common inventive link between the subject-matters of Inventions 1 and 2, the present application does not meet the requirements of Rule 13.1 PCT with respect to unity of invention, and is considered to consist of the two separate inventions given above.
- 5 The ISA has decided not to request additional fees. Thus an opinion is provided herein for both inventions.

Section V

- 1 Reference is made to the following documents:

- D1: LOPAREV ET AL: "Detection and differentiation of old world orthopoxviruses: restriction fragment length polymorphism of the crmB gene region." JOURNAL OF CLINICAL MICROBIOLOGY. JAN 2001, vol. 39, no. 1, pages 94-100
- D2: ROPP ET AL: "PCR strategy for identification and differentiation of small pox and other orthopoxviruses" JOURNAL OF CLINICAL MICROBIOLOGY, vol. 33, no. 8, August 1995, pages 2069-2076

2 Novelty (Art.33(2) PCT)

- 2.1 D1 discloses a method for the detection and differentiation of orthopoxviruses comprising the following steps (cf p.95, col.1, para.3 - col.2, para.1):
- adding to the sample each oligonucleotide of the primer pair VL2N and VL33 to amplify the crmB region of orthopoxviruses (cf also p.95, col.2, para.2);
 - adding to the PCR product a restriction enzyme NlaIII, AclI, NciI or Sau3A;
 - determining by gel electrophoresis if enzyme digestion has occurred.

The method of D1 therefore comprises all of the features of claims 1 and 2, thereby rendering said claims not novel.

- 2.2 The prior art does not disclose primer pairs comprising 12 or more consecutive nucleotides of SEQ ID NOS 1 and 2 or SEQ ID NOS 3 and 4. Therefore, the method of dependent claims 3 and 4 in which said primer pairs are used is novel.
- 2.3 Similarly, claim 5, directed to said primer pairs per se, and claims 6-8, directed to a kit comprising at least one of said primer pairs, appear to be novel.

3 Inventive step (Art.33(3) PCT)

- 3.1 The subject-matter of claims 3-8 differs from D1, relating to PCR-RFLP analysis of the crmB gene and from D2, relating to PCR-RFLP analysis of the HA gene, by the primer pairs used for the PCR amplification. Claim 3 further differs from D2 in the restriction enzymes used for the RFLP analysis.
- 3.2 The primer pairs defined by SEQ ID NOS 1 and 2 or 3 and 4 were designed by sequence alignment of all isolates of variola, monkeypox, camelpox, cowpox and vaccinia viruses; the amplicons they provide contain conserved restriction sites for

RFLP analysis, and the primer pairs allow highly sensitive detection of viral load (present description, p.9, l.31 - p.10, l.8).

- 3.3 The problem to be solved by claims 5-8 is the provision of primer pairs and kits comprising the same that result in more sensitive detection of orthopoxviruses. The solutions of SEQ ID NOS 1 and 2 for analysis of the HA gene or of SEQ ID NOS 3 and 4 for analysis using the crmB gene are not suggested in the prior art. Therefore, the subject-matter of claims 5 and 6-8 is considered to involve an inventive step.
- 3.4 The problem to be solved by claim 3 over D2 and by claim 4 over D1 is considered to be the provision of a more sensitive method for the detection and identification of orthopoxviruses. The solutions, namely the use of the primer pair defined by SEQ ID NOS 1 and 2 for targeting the HA gene or the primer pair defined by SEQ ID NOS 3 and 4 for the crmB gene, are considered to solve the problem only for certain embodiments covered by the claims, as only specific combinations of primer pairs and restriction enzymes will provide the desired result (Sau3AI and SpeI provide restriction patterns with the amplicon of the HA gene; DraI, Alw44I, SspI provide a banding pattern from the crmB gene: description, p.8, l.13-18).

Therefore, no inventive step can be acknowledged for claims 3 and 4, as the problem is not solved over the entire scope of the claims (cf also item VIII.2).

Section VIII

- 1 In the description, reference is made to restriction analysis using NlaIII enzyme in connection with Fig.1 (e.g. p.8, l.18-21; p.13, l.25-27); yet said figure does not show any restriction sites for NlaIII. Therefore, said reference is unclear (Art.6 PCT), as is the actual effect of using NlaIII, and the particular amplicon which it is used to digest.
- 2 Claim 1 is not supported by the description as required by Article 6 PCT, as its scope is broader than justified by the description and drawings. The reasons therefor are the following: said claim is directed to a method using at least one pair of primers directed to the HA or crmB gene of the orthopoxvirus genome and at least one restriction enzyme selected from Sau3AI, SpeI, DraI, HpaI, SspI, Alw44I

and NlaIII. However, none of these restriction enzymes would appear to produce a banding pattern for both target genes. Such a method is supported using only specific combinations of primer pairs and endonucleases.

The same objection applies to claims 2-4 and 7.